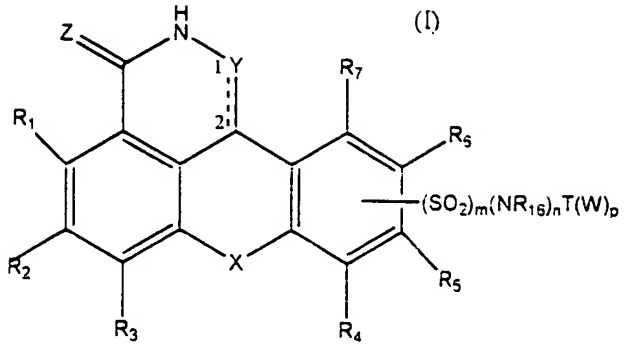
We claim:

1. A compound of Formula I:



(I)

or a pharmaceutically acceptable salt, hydrate, prodrug, or mixtures thereof, wherein:

m is zero or one;

n is zero or one;

p is one or two;

Y is a direct bond, >C=O, -O-, -N(R_{10})-, N, or - C(R_8)$_2$-;

Z is O, or S;

X is NR_{11}, -O-, -S-, C$R_{12}R_{13}$, a bond, -CR_{12}=CR_{13}-, or -C($R_{12}R_{13}$)C($R_{14}R_{15}$)-;

W is selected from -CN, -(N(R_9)$_2$) where the R_9 substituents may be combined to form a heteroaryl or cycloalkyl optionally containing at least one hetero atom, -P(O)$_2$-OR_9, -P(O)(OR_9)$_2$, -S(O)$_2$-R_9, -S(O)$_3R_9$, -C(O)-R_9, -C(O)-N(R_9)$_2$, -S(O)$_2$NR_9, cycloalkyl optionally containing at least one heteroatom, and heteroaryl;

R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_{12}, R_{13}, R_{14}, and R_{15} are independently: hydrogen, lower alkyl, cycloalkyl optionally containing at least one heteroatom, lower alkenyl, lower alkoxy, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroaryl, hydroxy, amino, nitro, halo, nitroso, sulfo, sulfonic acid or carboxy;

each R_9 is independently: hydrogen, lower alkyl, cycloalkyl optionally containing at least one heteroatom, lower alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, heteroaralkyl, hydroxy, lower alcohol, alkoxy, amino, or carboxy;

R_{10} and R_{11} are independently: hydrogen, lower alkyl, lower alkenyl, aryl, aralkyl, alkaryl, halo, hydroxy, alkoxy, amino, or carboxy;

each R_{16} is independently hydrogen or lower alkyl; and

T, when present, is a divalent or trivalent organic radical independently selected from the group consisting of: lower alkylene, lower alkenylene, arylene, aralkylene, and alkarylene;

wherein one, two or three of the hydrogen atoms of said divalent or trivalent organic radical can be substituted by a moiety selected from the group consisting of: lower (C_1-C_9 straight or branched chain) alkyl, cycloalkyl, lower (C_2-C_9 straight or branched chain) alkenyl, cycloalkenyl, aryl, heteroaryl, aralkyl, heteroaryalkyl, alkaryl, alkheteroaryl, halo, trifluoromethyl, hydroxy, lower (C_1-C_4) alkoxy, amino, nitro, trifluoromethyl, alkenyloxy, phenoxy, and benzyloxy;

wherein one, two, or three carbon atoms in the divalent or trivalent organic radical can be replaced by a hetero-atom-containing-moiety selected from the group consisting of: phenoxy, phenoxymethyl, phenoxycarbonyl, benzyloxy, -O-, >C=O, -S-, -SO_2-, -NR_1SO_2-, -SO_2NR_1-, -NR_1-, and -PO_2-;

wherein any of the lower (C_1-C_9 straight or branched chain) alkyl, C_3-C_8 cycloalkyl optionally containing at least one heteroatom in place of a carbon atom, lower (C_2-C_9 straight or branched chain) alkenyl, aryl, heteroaryl, aralkyl, and alkaryl groups can be independently substituted with one, two or three substituents selected from the group consisting of: lower (C_1-C_9 straight or branched chain) alkyl, C_3-C_8 cycloalkyl optionally containing at least one heteroatom in place of a carbon atom, lower (C_2-C_9 straight or branched chain) alkenyl, cycloalkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroaryl, halo, trifluoromethyl, hydroxy, lower (C_1-C_4) alkoxy, carboxy, carbonyl, lower alkyl ester, amino, nitro, trifluoromethyl, alkenyloxy, phenoxy, benzyloxy,

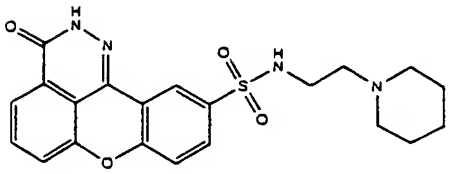
wherein one, two, or three carbon atoms of any of the lower (C_1-C_9 straight or branched chain) alkyl, C_3-C_8 cycloalkyl optionally containing at least one heteroatom in place of a carbon atom, lower (C_2-C_9 straight or branched chain) alkenyl, aryl, heteroaryl, aralkyl, and alkaryl groups can be replaced by a hetero-atom-containing-moiety selected from the group consisting of: -O-, >C=O, -S-, -SO_2-, -NR_1SO_2-, -SO_2NR_1-, N, -NR_1-, and -PO_2-.

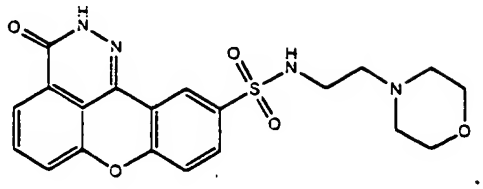
2. A compound of claim 1 wherein m and n are zero, p is one, W is -CN and R_1-R_7 are hydrogen.

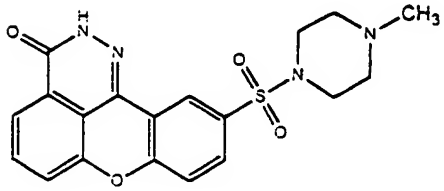
3. A compound of claim 1, wherein m and n are zero, p is one, W is -CN, T is -CH_2-, Z and X are oxygen, Y is N and R_1 to R_7 are hydrogen.

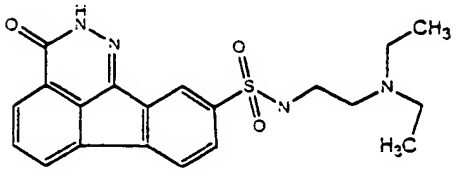
4. A compound of claim 1, wherein wherein p is one and W is -($N(R_9)_2$).

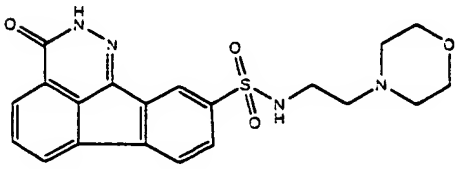
5. A compound of claim 4, selected from the group consisting of:

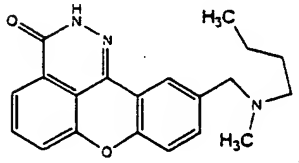


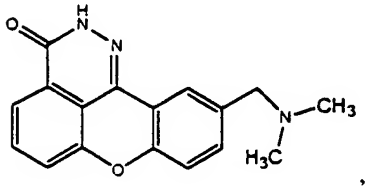


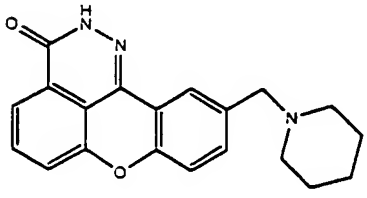


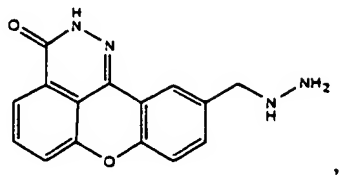


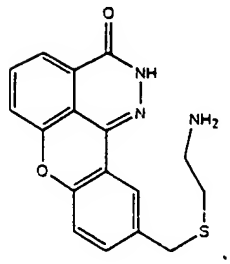


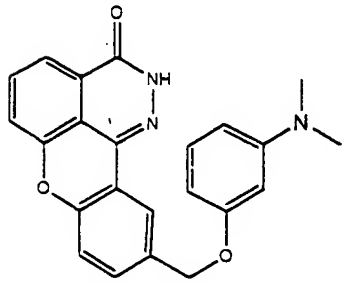


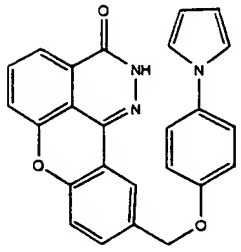


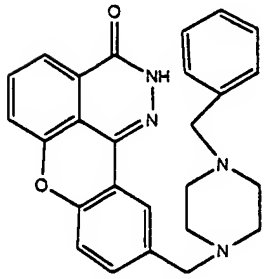


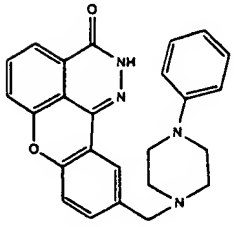


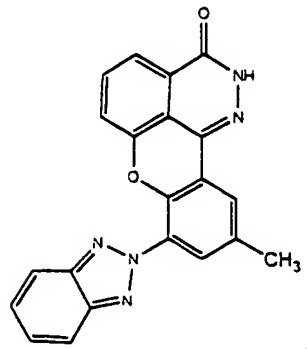


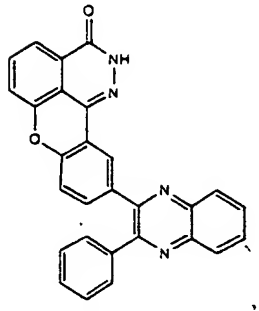


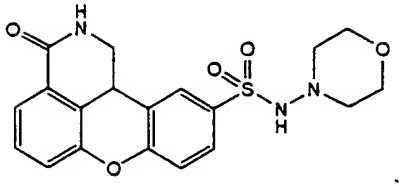


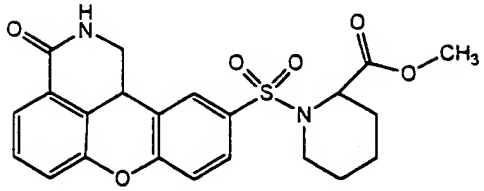


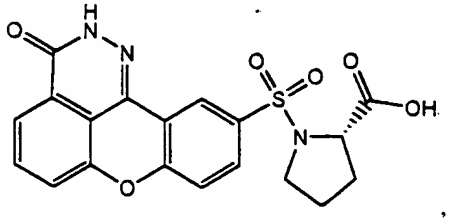


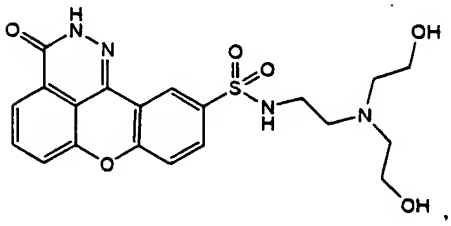


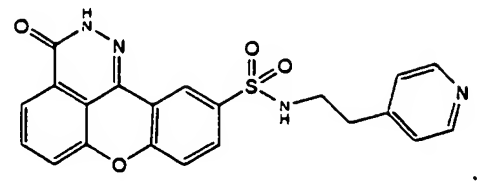


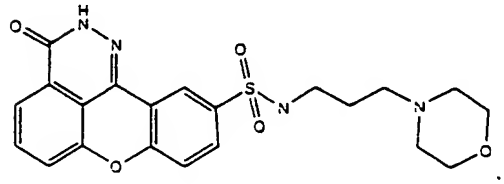


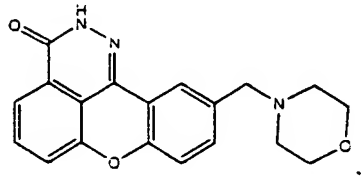


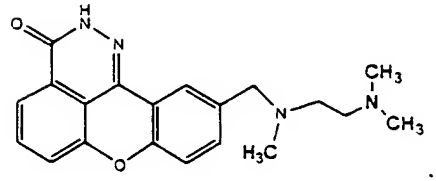


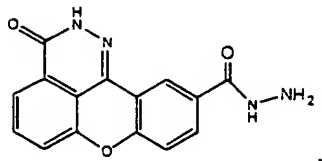


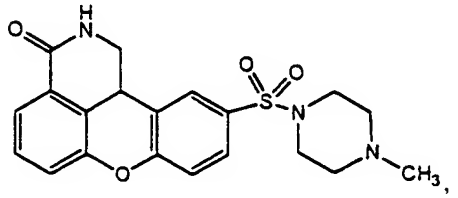


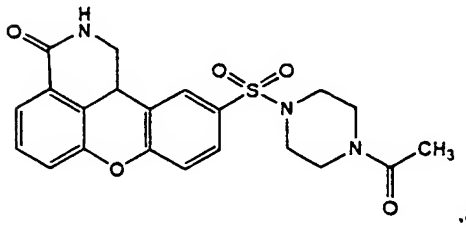








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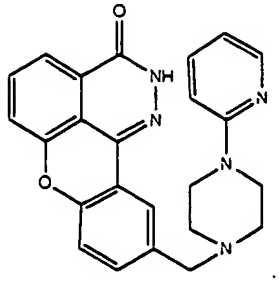
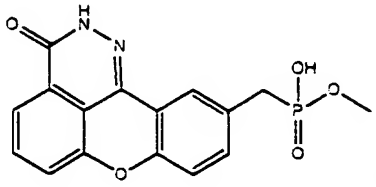


6. A compound of claim 1 wherein p is one and W is selected from the group consisting of -$P(O)_2$-OR_9 and -$P(O)(OR_9)_2$.

7. A compound of claim 6 selected from the group consisting of



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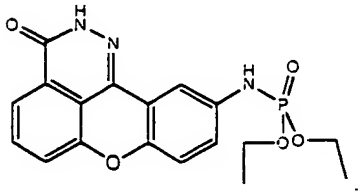
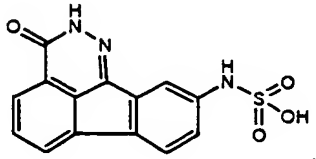
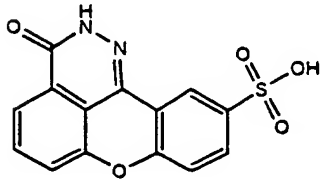
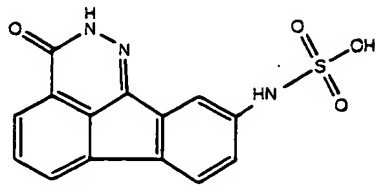


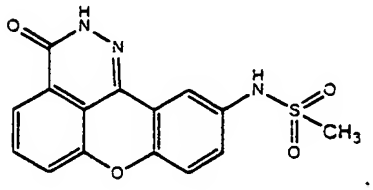
8. A compound of claim 1 wherein p is one and W is selected from the group consisting of -$S(O)_2$-R_9, -$S(O)_2OR_9$ and -$S(O)_2NR_9$.

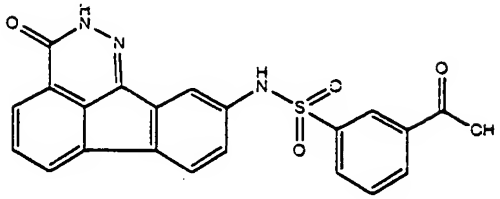
9. A compound of claim 8 selected from the group consisting of:

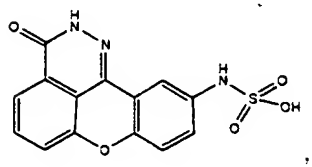


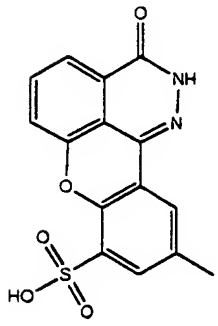


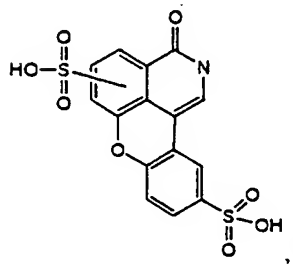








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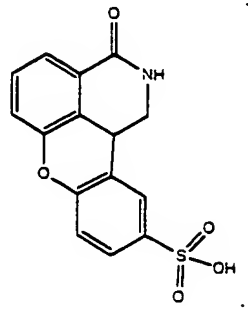
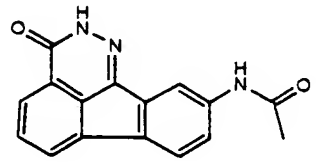
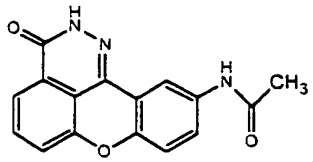
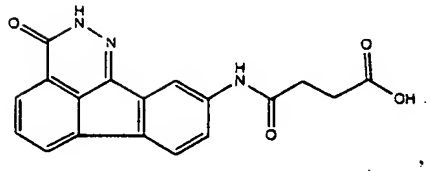


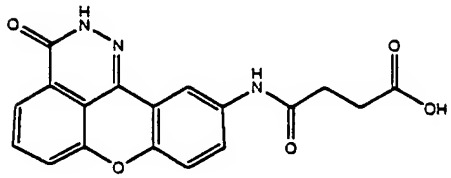
10. A compound of claim 1 wherein p is one and W is $-C(O)R_9$ or $-C(O)N(R_9)_2$.

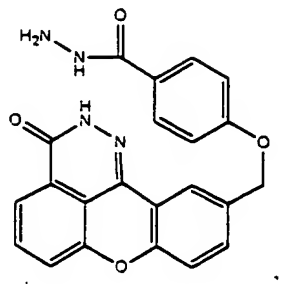
11. A compound of claim 10 selected from the group consisting of

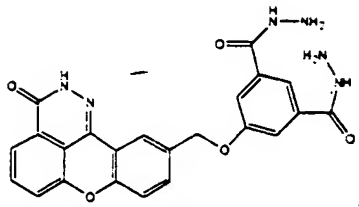


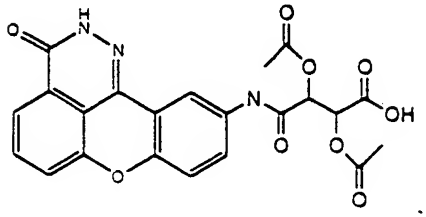


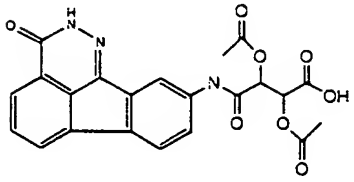


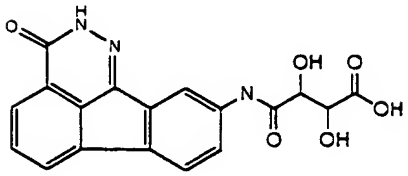


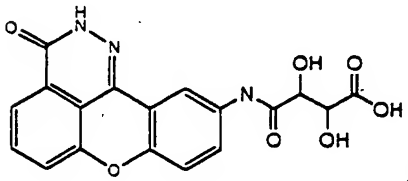




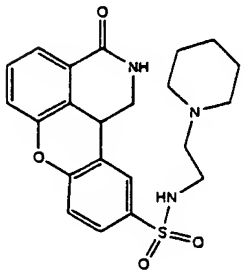






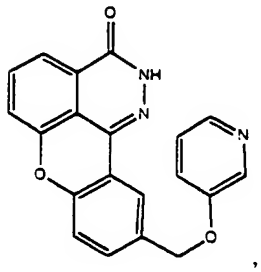


.and

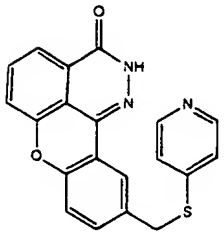


12. A compound of claim 1 wherein p is one and W is a heteroaryl or a cycloalkyl optionally containing at least one heteroatom.

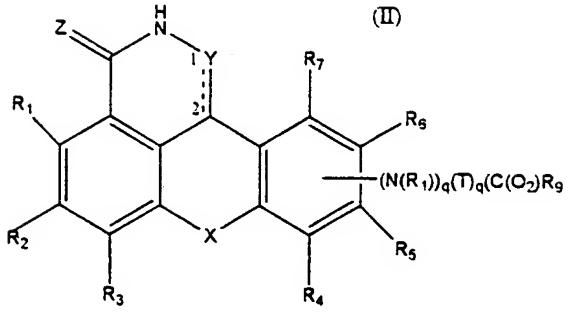
13. A compound of claim 12 selected from the group consisting of:



, and



14. A compound of Formula (II)



(II)

or a pharmaceutically acceptable salt, hydrate, prodrug, or mixtures thereof, wherein:

q is zero or one;

Y is N, -CH- or $-CH_2$;

Z is O;

X is -O-, or a bond;

R_1, R_2, R_3, R_4, R_5, R_6, and R_7 are independently: hydrogen, lower alkyl, lower alkenyl, cyloalkyl optionally containing at least one heteroatom, lower alkoxy, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroarly, hydroxy, amino, nitro, halo, nitroso, or carboxy;

R_9 is hydrogen, lower alkyl, cycloalkyl optionally containing at least one heteroatom, lower alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroaryl, hydroxy, alkoxy, amino, or carboxy; and

T, when present, is a divalent or trivalent organic radical independently selected from the group consisting of: lower alkylene, lower alkenylene, arylene, aralkylene, and alkarylene;

wherein one, two or three of the hydrogen atoms of said divalent or trivalent organic radical can be substituted by a moiety selected from the group consisting of: lower alkyl, lower alkenyl, aryl, aralkyl, alkaryl, halo, trifluoromethyl, hydroxy, alkoxy, amino, nitro, trifluoromethyl, alkenyloxy, phenoxy, and benzyloxy;

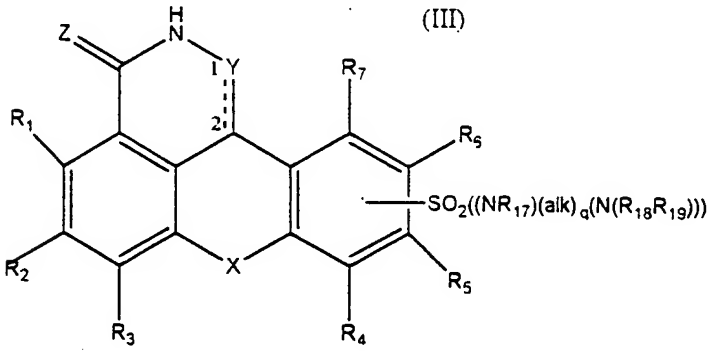
wherein one, two, or three carbon atoms in the divalent or trivalent organic radical can be replaced by a hetero-atom-containing-moiety selected from the group consisting of: penoxy, phenoxycarbonyl, benzyloxy, -O-, >C=O, -S-, $-SO_2-$, $-NR_1SO_2-$, $-SO_2NR_1-$, $-NR_1-$, and $-PO_2-$;

wherein the lower alkyl, cyloalkyl optionally containing at least one heteroatom, lower alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, and alkheteroaryl groups can be independently substituted with one, two or three substituents selected from the group consisting of:

lower alkyl, cycolalkyl optionally containing at least one heteratom, lower alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroaryl, halo, trifluoromethyl, hydroxy, alkoxy, carboxy, carbonyl, lower alkyl ester, amino, nitro, trifluoromethyl, alkenyloxy, phenoxy, benzyloxy,

wherein one, two, or three carbon atoms thereof can be replaced by a hetero-atom-containing-moiety selected from the group consisting of: -O-, >C=O, -S-, $-SO_2-$, $-NR_1SO_2-$, $-SO_2NR_1-$, $-NR_1-$, and $-PO_2-$.

15. A compound according to Formula (III)



(III)

wherein

Z and X are oxygen;

Y is N, -CH- or $-CH_2$;

q is zero or one;

"alk" is lower alkylene;

R_{17}, R_{18} and R_{19} are independently hydrogen or lower alkyl; or

R_{17} and R_{18} or R_{18} and R_{19} taken together can be a lower alkylene to form a heterocyclic ring; and

R_1, R_2, R_3, R_4, R_5, R_6 and R_7 are independently: hydrogen, lower alkyl, cycloalkyl optionally containing at least one hetero atom, lower alkenyl, lower alkoxy, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroaryl, hydroxy, amino, nitro, halo, nitroso, or carboxy.

16. A pharmaceutical composition which comprises: (i) a therapeutically effective amount of a compound according to claim 1 and (ii) a pharmaceutically acceptable carrier.

17. The pharmaceutical composition of claim 16, wherein the carrier is a sterile solution, suspension or emulsion, in a single or divided dose.

18. The pharmaceutical composition of claim 16, wherein the carrier is a capsule or tablet containing a single or divided dose of said compound.

19. The pharmaceutical composition of claim 16, wherein the carrier comprises a biodegradable polymer.

20. The pharmaceutical composition of claim 19, wherein the biodegradable polymer releases the compound of formula I over a prolonged period of time.

21. The pharmaceutical composition of claim 16, wherein the carrier is a solid implant.

22. The pharmaceutical composition of claim 16 for inhibiting PARP activity, treating or preventing diseases or disorders, altering gene expression, or radiosensitizing.

23. The pharmaceutical composition of claim 22, wherein the diseases or disorders are not mediated by NMDA toxicity.

24. The pharmaceutical composition of claim 22, wherein the diseases or disorders are selected from the group consisting of tissue damage resulting from cell damage or death due to necrosis or apoptosis, neuronal mediated tissue damage or diseases, neural tissue damage resulting from ischemia and reperfusion injury, neurological disorders and neurodegenerative diseases, vascular stroke, cardiovascular disorders, age-related muscular degeneration, AIDS and other immune senescence diseases, arthritis, atherosclerosis, cachexia, cancer, degenerative diseases of skeletal muscle involving replicative senescence, diabetes, head trauma, immune senescence, inflammatory bowel disorders, muscular dystrophy, osteoarthritis, osteoporosis, chronic pain, acute pain, neuropathic pain, nervous insult, peripheral nerve injury, renal failure, retinal ischemia, septic shock, and

skin aging, diseases or disorders relating to lifespan or proliferative capacity of cells, and diseases or disease conditions induced or exacerbated by cellular senescence.

25. The pharmaceutical composition of claim 24, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic brain injury, physical damage to the spinal cord, stroke associated with brain damage, and demyelinating diseases.

27. The pharmaceutical composition of claim 25, wherein the peripheral neuropathy is caused by Guillain-Barre syndrome.

28. The pharmaceutical composition of claim 25, wherein the demyelinating disease is multiple sclerosis.

29. The pharmaceutical composition of claim 24, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease and amyotropic lateral sclerosis.

30. The pharmaceutical composition of claim 24, wherein the cancer is selected from the group consisting of ACTH-producing tumors, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervix cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hairy cell leukemia, head & neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and/or non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, non-Hodgkin's lymphoma, osteosarcoma, ovary cancer, ovary (germ cell) cancer, prostate cancer, pancreatic cancer, penile cancer, retinoblastoma, skin cancer, soft-tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, cancer of the uterus, vaginal cancer, cancer of the vulva and Wilm's tumor.

31. The pharmaceutical composition of claim 24, wherein the bowel disorder is colitis.

32. The pharmaceutical composition of claim 24, wherein the bowel disorder is Crohn's disease.

33. The pharmaceutical composition of claim 24, wherein the cardiovascular disorder is selected from the group consisting of cardiovascular tissue damage, coronary artery disease, myocardial infarction, angina pectoris and cardiogenic shock.

34. The pharmaceutical composition of claim 24, wherein the septic shock is endotoxic shock.

35. The pharmaceutical composition of claim 24, wherein the disease or disease condition induced or exacerbated by cellular senescence is selected from the group consisting of skin aging, Alzheimer's disease, atherosclerosis, osteoarthritis, osteoporosis, muscular dystrophy, age-related muscular degeneration, immune senescence, and AIDS.

36. A method of inhibiting PARP activity, treating or preventing diseases or disorders, altering gene expression, or radiosensitizing, comprising: administering a therapeuticaly effective amount of a compound of claim 1.

37. The method of claim 36, wherein the compound is administered as a sterile solution, suspension or emulsion, in a single or divided dose.

38. The method of claim 36, wherein the compound is administered as a capsule or tablet containing a single or divided dose of said compound.

39. The method of claim 36, wherein the compound is administered with a biodegradable polymer.

40. The method of claim 39, wherein the biodegradable polymer releases the compound of formula I over a prolonged period of time.

41. The method of claim 36, wherein the compound is administered with a solid implant.

42. The method of claim 36, wherein the diseases or disorders are not mediated by NMDA toxicity.

43. The method of claim 36, wherein the diseases or disorders are selected from the group consisting of tissue damage resulting from cell damage or death due to necrosis or apoptosis, neuronal mediated tissue damage or diseases, neural tissue damage resulting from ischemia and reperfusion injury, neurological disorders and neurodegenerative diseases, vascular stroke, cardiovascular disorders, age-related muscular degeneration, AIDS and other immune senescence diseases, arthritis, atherosclerosis, cachexia, cancer, degenerative diseases of skeletal muscle involving replicative senescence, diabetes, head trauma, immune senescence, inflammatory bowel disorders, muscular dystrophy, osteoarthritis, osteoporosis, chronic pain, acute pain, neuropathic pain, nervous insult, peripheral nerve injury, renal failure, retinal ischemia, septic shock, and

skin aging, diseases or disorders relating to lifespan or proliferative capacity of cells, and diseases or disease conditions induced or exacerbated by cellular senescence.

44. The method of claim 43, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic brain injury, physical damage to the spinal cord, stroke associated with brain damage, and demyelinating diseases.

45. The method of claim 44, wherein the peripheral neuropathy is caused by Guillain-Barre syndrome.

46. The method of claim 44, wherein the demyelinating disease is multiple sclerosis.

47. The method of claim 43, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease and amyotropic lateral sclerosis.

48. The method of claim 43, wherein the cancer is selected from the group consisting of ACTH-producing tumors, acute lymphocytic leukemia, acute nonlymphocytic leukemia, cancer of the adrenal cortex, bladder cancer, brain cancer, breast cancer, cervix cancer, chronic lymphocytic leukemia, chronic myelocytic leukemia, colorectal cancer, cutaneous T-cell lymphoma, endometrial cancer, esophageal cancer, Ewing's sarcoma, gallbladder cancer, hairy cell leukemia, head & neck cancer, Hodgkin's lymphoma, Kaposi's sarcoma, kidney cancer, liver cancer, lung cancer (small and/or non-small cell), malignant peritoneal effusion, malignant pleural effusion, melanoma, mesothelioma, multiple myeloma, neuroblastoma, non-Hodgkin's lymphoma, osteosarcoma, ovary cancer, ovary (germ cell) cancer, prostate cancer, pancreatic cancer, penile cancer, retinoblastoma, skin cancer, soft-tissue sarcoma, squamous cell carcinomas, stomach cancer, testicular cancer, thyroid cancer, trophoblastic neoplasms, cancer of the uterus, vaginal cancer, cancer of the vulva and Wilm's tumor.

49. The method of claim 43, wherein the bowel disorder is colitis.

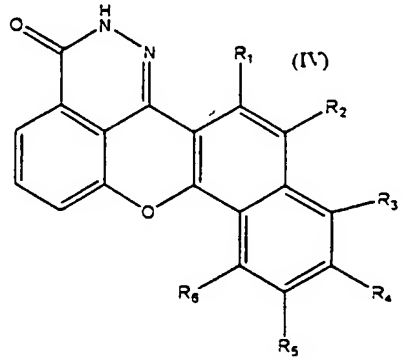
50. The method of claim 43, wherein the bowel disorder is Crohn's disease.

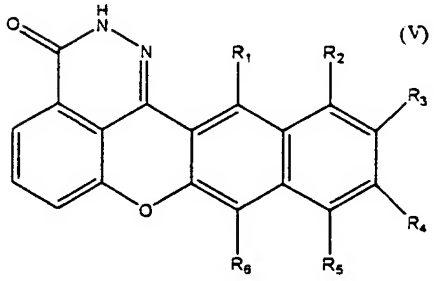
51. The method of claim 43, wherein the cardiovascular disorder is selected from the group consisting of cardiovascular tissue damage, coronary artery disease, myocardial infarction, angina pectoris and cardiogenic shock.

52. The method of claim 43, wherein the septic shock is endotoxic shock.

53. The method of claim 43, wherein the disease or disease condition induced or exacerbated by cellular senescence is selected from the group consisting of skin aging, Alzheimer's disease, atherosclerosis, osteoarthritis, osteoporosis, muscular dystrophy, age-related muscular degeneration, immune senescence, and AIDS.

54. A compound according to Formula (IV) or Formula (V)





wherein, R_1, R_2, R_3, R_4, R_5, and R_6, are independently: hydrogen, lower alkyl, lower alkenyl, cyloalkyl optionally containing at least one heteroatom, lower alkoxy, aryl, heteroaryl, aralkyl, heteroaralkyl, alkaryl, alkheteroarly, hydroxy, amino, nitro, halo, nitroso, or carboxy.